

AD-A105 002

CALIFORNIA UNIV BERKELEY SCHOOL OF PUBLIC HEALTH  
DEVELOPMENT OF AN AIR SAMPLING AND ANALYTICAL METHOD FOR 1,6-HE--ETC(U)  
JUL 81 S M RAPPAPORT.

F/G 7/4

AFOSR-80-0113

UNCLASSIFIED

AFOSR-TR-81-0666

NL

1 or 1  
AFOSR-  
AF-000

END  
DATE FILMED  
10-81  
OFC

AFOSR-TR- 81 -0666

(12)

AD A105002

Final Research Report

for

AFOSR GRANT ■ AFOSR-80-0113

entitled

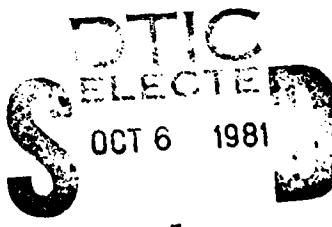
DEVELOPMENT OF AN AIR SAMPLING AND ANALYTICAL METHOD FOR 1, 6-HEXAMETHYLENE DIISOCYANATE

by

Stephen M. Rappaport

University of California, Berkeley, CA 94720

DTIC FILE COPY



Approved for public release;  
distribution unlimited.

029

SECURITY CLASSIFICATION OF THIS PAGE (When Data Entered)

19. REPORT DOCUMENTATION PAGE

LEAD INSTRUCTIONS  
BEFORE COMPLETING FORM

18. REPORT NUMBER AFOSR-TR-81-0666

12. GOVT ACCESSION NO. AD-A105002

3. RECIPIENT'S CATALOG NUMBER (9)

4. TITLE (and Subtitle)  
DEVELOPMENT OF AN AIR SAMPLING AND ANALYTICAL METHOD  
FOR 1,6-HEXAMETHYLENE DIISOCYANATE

5. TYPE OF REPORT & PERIOD COVERED  
Final report

7. AUTHOR(s)

Stephen M. Rappaport

6. PERFORMING ORG. REPORT NUMBER

8. CONTRACT OR GRANT NUMBER(s)

AFOSR-80-0113

9. PERFORMING ORGANIZATION NAME AND ADDRESS

School of Public Health  
University of California  
Berkeley, CA 94720

10. PROGRAM ELEMENT, PROJECT, TASK AREA & WORK UNIT NUMBERS

61102F  
Q312/009

11. CONTROLLING OFFICE NAME AND ADDRESS

Air Force Office of Scientific Research /NL  
Bolling AFB, D.C. 20332

12. REPORT DATE

81 July 10

13. NUMBER OF PAGES

33

14. MONITORING AGENCY NAME & ADDRESS (if different from Controlling Office)

16. DISTRIBUTION STATEMENT (of this Report)

Approved for public release;  
distribution unlimited.

11 10 Jul 81

17. DISTRIBUTION STATEMENT (of the abstract entered in Block 20, if different from Report)

18. SUPPLEMENTARY NOTES

19. KEY WORDS (Continue on reverse side if necessary and identify by block number)

ISOCYANATES, AIR SAMPLING, IMPREGNATED FILTERS, LIQUID CHROMATOGRAPHY

20. ABSTRACT (Continue on reverse side if necessary and identify by block number)

A preliminary evaluation of a new air sampling and analytical procedure for 1,6-hexamethylenediisocyanate (HDI) is given. Airborne HDI is trapped by drawing air through a filter which had been impregnated with 1-naphthylene methyl amine (NMA). HDI and NMA react on the filter surface to form the stable urea, HDI-NMA, which is quantified by HPLC. A novel procedure is presented for separating HDI-NMA from NMA during analysis. Preliminary data suggest that the procedure will be appropriate for evaluating airborne exposures to HDI in either 10 min or 4-hr air samples with detection limits of 2.2 ppb and 0.09 ppb respectively.

DD FORM JAN 73 1473

SECURITY CLASSIFICATION OF THIS PAGE (When Data Entered)

400144

400144

## INTRODUCTION

During the summer of 1979 the principal investigator participated in the USAF Summer Faculty Research Program at the School of Aerospace Medicine, Brooks AFB, Texas. The purpose of that project was to determine the viability of an air sampling and analytical method for those diisocyanates which are used by the Air Force in polyurethane foams and paints. The work was justified on the grounds that the Air Force uses extremely large quantities of polyurethane paints and somewhat smaller quantities of polyurethane foams in various operations. Thus the likelihood is great that exposures to toxic diisocyanates could occur among personnel of the Air Force and its contractors. Since existing methods for the measurement of airborne diisocyanates are fraught with pitfalls, a new and presumably better procedure is clearly needed by industrial hygienists in the Air Force to evaluate the degree of hazard posed to personnel by these exposures.

A report of the summer project, attached as the Appendix, describes a new air sampling and analytical procedure which showed promise for the quantification of airborne diisocyanates. The sampler consisted of a glass-fiber filter which had been impregnated with the chromophore-containing amine, 1-naphthylene methyl amine (NMA). As air from the environment is drawn through the filter NMA reacts rapidly with the diisocyanate to produce a urea which is nonvolatile and stable prior to analysis. The urea is dissolved in  $\text{CH}_3\text{OH}$  and analyzed by high performance liquid chromatography (HPLC) using a reversed-phase system and a UV detector at 223 nm. The analytical procedure can differentiate among ureas formed from reactions of various diisocyanates with NMA and is not subject to interference by amines or other impurities which may be present in the environment.

Dist	Avail and/or Special
A	

STATEMENT OF WORK

Preliminary work conducted by the principal investigator indicated that the diisocyanate, 1,6-hexamethylenediisocyanate (HDI), could be quantitatively converted to its urea (HDI-NMA) on the surface of a filter impregnated with NMA and that HDI-NMA could be recovered in high yield. The fact that HDI is used extensively by the Air Force in paints for aircraft and vehicles made the investigation of this compound attractive. Furthermore, because HDI is an aliphatic diisocyanate of relatively high vapor pressure and low reactivity, it represented a "worst case" whose successful measurement in air samples would suggest the method to be suitable for other diisocyanates as well.

The current study was performed to validate the proposed method for HDI. If successful, future studies could be directed towards the whole range of diisocyanates used by the Air Force. Specifically, the research was designed to achieve the following goals:

1. Test the sampling method with dynamic test atmospheres of HDI for both long and short-term sampling intervals.
2. Determine whether humidity influences the collection characteristics of the sampler.
3. Determine the storage stability of the samplers and ureas after collection.
4. Determine the absolute sensitivity of the analytical procedure.
5. Streamline the chromatographic analysis to reduce the time required to elute excess NMA from the column.

STATUS OF THE RESEARCH EFFORT

Because of unanticipated problems associated with the production of controlled test atmospheres it was not possible to meet all of the proposed goals of the research. Goals 4 and 5 dealing with the analytical methods were achieved and will be described in detail. However, goals 1-3 related to the validation of the sampling methods were dependent upon the test atmospheres and therefore were only partially achieved. Although it is disappointing that the goals could not be completely realized during the scheduled (and extended) period of the grant, work is still in progress and will be pursued to completion. In addition, a series of air samples were collected during the spraying of aircraft by Air Force personnel at Mather AFB, using filters which had been supplied by the investigator. These samples will be analyzed by the investigator to determine their HDI-NMA content. A supplemental report covering the results of the continuing experiments will be submitted to AFOSR at a future date.

Reduction of Analysis Time

The analytical method developed in this project allows the sensitive and specific measurement of HDI (as HDI-NMA) in air samples. Levine *et al* (1) originally reported the use of NMA as a reactant for diisocyanates. (Samples were collected by liquid absorption in impingers containing a toluene solution of NMA.) Because it is a relatively basic primary amine and because the amino group is separated from the naphthylene moiety by a methylene carbon (reducing steric effects), NMA reacts rapidly with aliphatic diisocyanates such as HDI. Indeed it is this high reactivity of NMA and isocyanates which allows HDI to be trapped on the surface of a filter

during air sampling. However, the chemically-basic character of NMA presents a problem to the analyst. Since excess NMA (from the filter) is present in a quantity which is large relative to the HDI-NMA content it must be removed from HDI-NMA prior to or during HPLC analysis. It was observed by Levine et al (1) and confirmed by the investigator (see Appendix) that NMA eluted extremely slowly from the reversed-phase column used in the analysis ( $\mu$  Bondapak-C<sub>18</sub>, Waters Associates) resulting in analysis times in the range of 1 hr. It was therefore desirable to seek a means of eluting NMA from the system more quickly to reduce the time required for analysis.

The first efforts to reduce analysis time focused upon the strength of the eluting solvent. Solutions containing NMA and HDI-NMA were analyzed using various ratios of H<sub>2</sub>O/CH<sub>3</sub>OH as the eluting solvent. NMA always eluted very slowly (45-90 min) in a broad peak regardless of the ratio of H<sub>2</sub>O/CH<sub>3</sub>OH. Since NMA is more polar than HDI-NMA it would theoretically elute more quickly than the urea in a reversed-phase system. Since this was clearly not the case it was concluded that NMA was being retained because of a strong attraction between its basic amino group and residual silanol (Si-OH) groups present on the silica backbone of the C<sub>18</sub> bonded phase.

[Note: C<sub>18</sub> columns are prepared by reacting silanol groups with C<sub>18</sub> containing molecules. Since complete coverage is never achieved, residual silanol groups are present in the column and would be expected to strongly adsorb the basic NMA.]

A relatively rapid analytical procedure was developed by adding a micro-particle C<sub>18</sub> (Rheodyne, Cotati, CA) to strip NMA from the urea during HPLC analysis. By using two 6-port switching valves it was possible to then

backflush NMA to the detector prior to elution of HDI-NMA as shown in Figure 1. The sample is injected into the system and flows first to the precolumn. The urea passes quickly through the precolumn to the analytical column while the amine is retained by the precolumn. This requires 1.5 minutes at a flow rate of 1 mL/min. The solvent flow is then redirected using the valve so that it flows first through the analytical column then back through the precolumn in the opposite direction. This backflushes the amine off the precolumn through the detector prior to the elution of the urea through the analytical column and the precolumn. This backflushing procedure reduces analysis time to about fifteen minutes while still achieving separation of NMA and HDI-NMA. Analysis time may be even further reduced by increasing the flow rate of the mobile phase. Figure 2 shows chromatograms of samples containing NMA and either HDI-NMA or TDI-NMA (the urea of toluene 2,4-diisocyanate). The conditions were as follows: Pump - Altex Model 100; Detector - Perkin Elmer Model LC-75 at 223 nm, 0.08 AUFS; Mobile Phase - 25% H<sub>2</sub>O/CH<sub>3</sub>OH at 1 mL/min; Injection Volume - 20 µL; Valve configuration as shown in Figure 1. The retention times for HDI-NMA and TDI-NMA were approximately 10 min and 12 min respectively.

#### Analytical Procedure

The analytical procedure for determination of HDI-NMA in air samples is as follows. Glass-fiber filters (37 mm, Type AP40, Millipore) are impregnated by dipping them momentarily in a CH<sub>2</sub>Cl<sub>2</sub> solution containing 200 µg/mL of NMA (Aldrich Chemical Co.). Each filter absorbs approximately 0.8 mL of solution or 160 µg of NMA. Filters are placed on a wire rack to dry for a few minutes and stored in desiccated glass containers at -4°C prior to use. Filters are placed in acrylic 37-mm, in-line filter cassettes for

sampling.

After sampling filters are removed from the cassettes, folded, and placed in glass centrifuge tubes. Approximately 3.5 mL of  $\text{CH}_2\text{Cl}_2$  (enough to cover the filters) are added to the tubes which are capped and placed in an ultrasonic bath at 40°C for 30 min. [This step allows any unreacted isocyanate groups to react with NMA in solution.] The solvent is then removed by evaporation under dry  $\text{N}_2$  at 40°C. Then 3.0 mL of  $\text{CH}_3\text{OH}$  are added to each tube which is capped and placed in an ultrasonic bath at 40°C for 50 min. [Sonication is required to dissolve HDI-NMA which is only slightly soluble ( $\sim 8 \mu\text{g/mL}$ ) in  $\text{CH}_3\text{OH}$ .] Filters are then compressed to the bottom of the tube with a clean glass rod and the samples are centrifuged at  $\sim 1500$  rpm for 1 min. A 20  $\mu\text{L}$  aliquot is carefully removed from the supernatant for injection into the HPLC.

Standards are prepared by placing several impregnated filters in centrifuge tubes and adding  $\sim 3.5$  mL of  $\text{CH}_2\text{Cl}_2$ . Aliquots of a freshly prepared  $\text{CH}_2\text{Cl}_2$  solution of HDI are added to the tubes with a 10- $\mu\text{L}$  syringe. Standards are then sonicated, dried under  $\text{N}_2$ , and prepared for analysis as described above. [Note: it is important that standards be prepared with filters from the same batch used for sampling to ensure comparable integration of the HDI-NMA peak on the tailing NMA peak. See Figure 2.] Peak areas were integrated in this study with a Perkin Elmer Model M-1 digital integrator.

All solvents were distilled in glass (Burdick and Jackson). 1,6-HDI (ACS reagent grade) was obtained from Eastman.

### Limits of Detection and Quantification

Using the analytical procedure given above for a series of standards the limits of detection and quantification of the method were estimated. At a detector range of 0.02 AUFS the peak to peak noise level on our chromatograms was about 0.5% of full scale. Given the criterion of a detection limit having a signal to noise ratio of 3 a peak of 1.5% of full scale would be required for detection. This corresponds to 0.15  $\mu\text{g}$  HDI per sample. Assuming that a quantification limit requires a signal to noise ratio of about 10 or 5% of full scale, 0.34  $\mu\text{g}$  of HDI could be quantified.

If HDI were quantitatively recovered from impregnated filters the above limits suggest that the detection limit of HDI in a 10 L air sample (10 min at 1 L/min) would be 15  $\mu\text{g}/\text{m}^3$  (2.2 ppb) and the quantification limit would be 34  $\mu\text{g}/\text{m}^3$  (5.0 ppb). These levels are well below the standard recommended by NIOSH (2) for short term exposure to HDI which is 140  $\mu\text{g}/\text{m}^3$  for 10 min. The corresponding air concentrations which could be detected in 240 L samples (4 hr at 1 L/min) include a detection limit of 0.63  $\mu\text{g}/\text{m}^3$  (0.09 ppb) and a quantification limit of 1.4  $\mu\text{g}/\text{m}^3$  (0.21 ppb). Thus, it seems likely that the analytical method described herein has ample sensitivity to allow the evaluation of either short or long-term exposures to HDI at the current levels recommended by NIOSH.

### Air Sampling

Preliminary experiments with air sampling were performed by spiking filters with airborne HDI as shown in Figures 3 and 4. Impregnated filters were placed in 37-mm in-line cassettes through which air was drawn at 1 L/min. Flow rates were controlled with critical orifices. Aliquots of a few  $\mu\text{L}$  of a freshly prepared  $\text{CH}_2\text{Cl}_2$  solution of HDI were injected onto the

walls of glass inlet tubes which had been inserted into the entry sections of the filter cassettes (see Figure 4). Fourteen filters were spiked in this manner with 3.8 µg of HDI. Room air was drawn through the filters for 30 min to ensure complete vaporization of HDI from the inlet tubes. In a parallel experiment, 14 impingers containing 10 mL of a  $10^{-4}$ M toluene solution of NMA were also spiked with 3.8 µg of HDI. Flow rates through the impingers were also controlled at 1 L/min for 30 min.

After sampling filters were removed from their cassettes and analyzed as described above against 14 standards prepared from impregnated filters. Impinger samples were analyzed by drying the toluene under  $N_2$  at 60°C and dissolving the samples in  $CH_3OH$  as described for the filters. Fourteen impinger standards were prepared by adding 3.8µg of HDI to 10 mL portions of a  $10^{-4}$ M toluene solution of NMA and were analyzed as described above.

Results for this experiment are given in Table I. The average recovery of HDI-NMA from filters was 93% of standard values. This can be compared with a corresponding recovery of HDI-NMA from impingers of 76%. This suggests that HDI-NMA is produced on and can be recovered from impregnated filters in high yield and that sampling results should compare favorably, i.e., should have no more negative bias than samples collected by liquid absorption in impingers. Indeed it appears from this preliminary experiment that HDI-NMA can be recovered in higher yield from impregnated filters than from impingers.

The further evaluation of the sampling method required the establishment of controlled test atmospheres of known air concentration. Considerable difficulty was encountered in producing such test atmospheres. Initial

experiments designed to continuously inject organic solutions of HDI into a moving air stream were totally unsuccessful. Refinements in which both the air stream and the injection zone were heated were equally unsuccessful. Attempts to generate vapors of HDI from conventional diffusion tubes at elevated temperatures (75-100°C) resulted in the apparent polymerization or degradation of HDI in the diffusion cell. Finally, after obtaining an extension of the period of the grant from AFOSR a permeation oven was purchased (using University funds) and attempts were made to generate HDI by permeation through the walls of silicone tubing as described by Dharmarajan and Rando (3). After some effort, this procedure did in fact allow the reproducible generation of HDI.

A Metronics Model 340 permeation chamber was used. HDI permeated through the walls of a 7-mm section of Mannosil tubing (1/4"-i.d., 3/32" wall thickness, Monnostat Inc., New York) at a rate of 16 µg/min at 35°C. Vapor was swept from the permeation chamber by dry air through Teflon tubing to a Teflon chamber where the vapor was diluted with air. Samples can be withdrawn from the diluted air stream through either impregnated filters or impingers.

Experiments are currently in progress to evaluate the sampling procedure with the controlled test atmospheres. Tests will be performed over a range of air concentrations for both short-term (10 min) and long term (4 hr) sampling intervals. Tests will also be conducted to determine the effects of both humidity and storage upon sampling.

The investigator is enthusiastic about the ultimate success of the effort and hopes to complete this preliminary project this summer. It is always disappointing when a project's goals cannot be realized as originally scheduled. However, the difficulties posed by certain seemingly straight-forward procedures were totally unanticipated. It should be emphasized that the novel sampling approach used in this work is simpler and immensely more useful to the industrial hygienist than other methods currently available. It also appears likely that if the method is indeed found suitable for HDI (a worst case), as is indicated by this report, it may be applied to virtually all other diisocyanates used by the Air Force.

#### References

1. Levine, S.P., Hoggatt, J.H., Chladek, E., Jungclaus, G. and Gerlock, J.L.: "Determination of Aliphatic Isocyanates in Air by a Liquid-Chromatographic Fluorescence Technique," Anal. Chem. 51:1106-1109 (1979).
2. Criteria for a Recommended Standard... Occupational Exposure to Diisocyanates. USDHEW (NIOSH) publication No. 78-215, USGPO, Washington, DC, 1978.
3. Dharmarajan, V. and Rando, R.J.: "A New Method for the Generation of Standard Atmospheres of Organo Isocyanates," Am. Ind. Hyg. Assoc. J. 40:870-875 (1979).

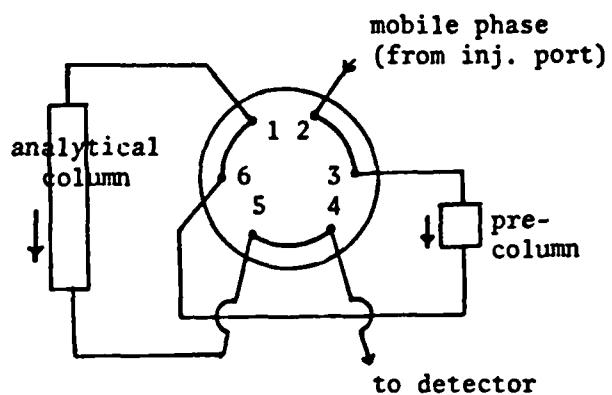
PROFESSIONAL PERSONNEL ASSOCIATED WITH THE RESEARCH

In addition to the principal investigator, three other individuals have been involved with the work. Two graduate students, Ms. B. Gayle Goff and Ms. Martha Waters, have performed their Masters' research on the problem. Ms. Goff submitted a thesis which dealt primarily with the development of the analytical procedure for HDI-NMA and TDI-NMA (Microdetermination of Isocyanates in Air by Impregnated Filter Collection and HPLC Analysis, October, 1980). Ms. Waters is currently involved with the validation of the sampling method. The third individual, Mr. Konstantin Zaharoff, is a Staff Research Associate. He participated primarily on the production of controlled test atmospheres of HDI in air.

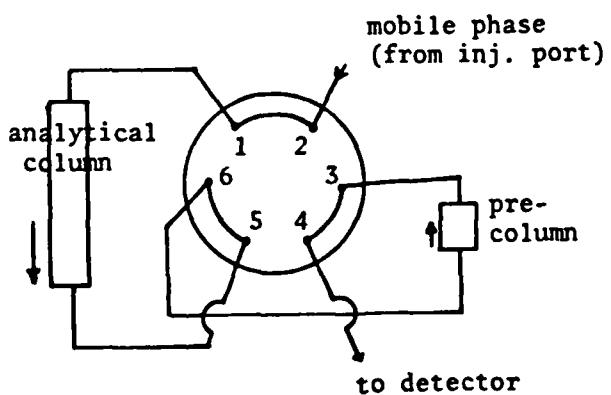
TABLE I  
RECOVERY\* OF HDI FROM SPIKED FILTERS AND IMPINGERS

Sample Type	Mean Peak Area (counts)	Std. Dev.	R.S.D. (%)	Sample Recovery (%)
Filter Standards	82428	7090	8.6	-
Filter Samples	76410	11230	14.7	93
Impinger Standards	79686	11812	14.8	-
Impinger Samples	60727	12745	21.0	76

\*14 standards and samples per group; each standard and sample were spiked with 3.8 µg of HDI.



## INJECTION



## BACKFLUSH PRECOLUMN

Figure 1. Switching valve configuration for analysis of NMA and HDI-NMA

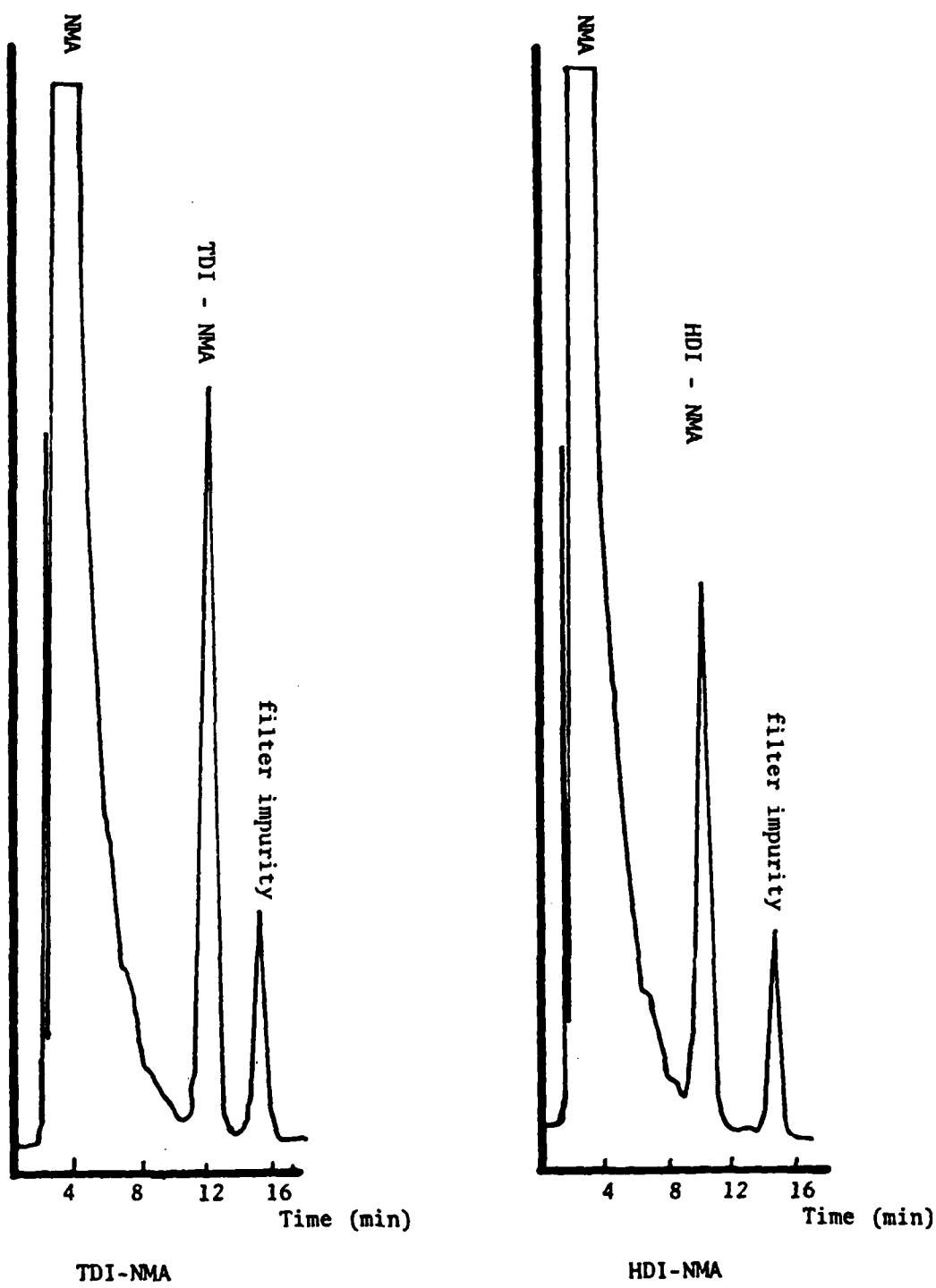


Figure 2. HPLC chromatograms of NMA and HDI-NMA and TDI-NMA using conditions given in the text

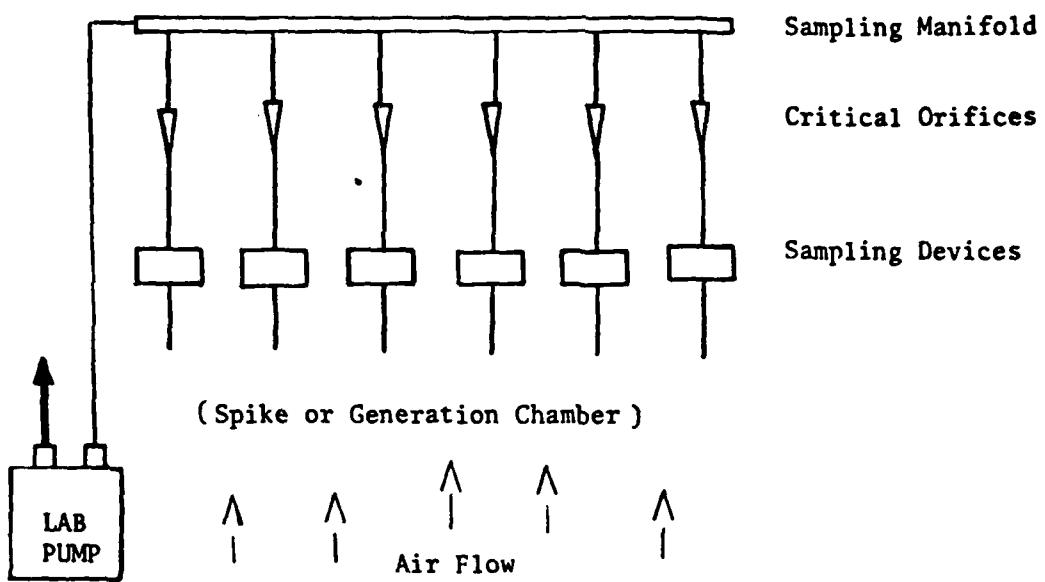


Figure 3. Laboratory sampling arrangement

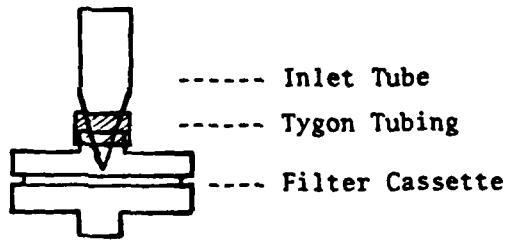


Figure 4. Filter spiking arrangement

APPENDIX

1979 USAF-SCEEE SUMMER FACULTY RESEARCH PROGRAM

Sponsored by the

AIR FORCE OFFICE OF SCIENTIFIC RESEARCH

Conducted by the

SOUTHEASTERN CENTER FOR ELECTRICAL ENGINEERING EDUCATION

FINAL REPORT

DEVELOPMENT OF AN AIR-SAMPLING AND ANALYTICAL

METHOD FOR DIISOCYANATES

Prepared by: Stephen M. Rappaport, Ph.D.

Academic Rank: Assistant Professor

Department and University:

Department of Biomedical and Environmental Health Sciences  
University of California, Berkeley

Research Location: USAF School of Aerospace Medicine

Crew Protection Branch

Brooks AFB, Texas

USAF Research Colleagues: Dr. Richard Miller, Major James Rock.

Contract No.: F 49620-79-C-0038

DEVELOPMENT OF AIR-SAMPLING AND ANALYTICAL METHOD  
FOR DIISOCYANATES

Stephen M. Rappaport

A method has been developed for the collection and analysis of diisocyanates in air. Air is drawn through a filter impregnated with 1-naphthylenemethylamine (NMA) which reacts with the diisocyanate to produce a stable urea. The method should be suitable for the collection of diisocyanates in either vapor or aerosol form. The urea is dissolved in methanol and analyzed by high performance liquid chromatography (HPLC). The method was evaluated with 1,6-hexamethylene diisocyanate (HDI). Results indicated HDI vapor to be efficiently trapped by the filter. Analysis gave a quantitation limit of ~2ng/ injection which allows airborne HDI to be measured at 0.002ppm in a 10-L air sample. Additional development should reduce the limit of quantitation and simplify the analysis.

#### ACKNOWLEDGEMENTS

The author would like to thank the Air Force Systems Command, the Air Force Office of Scientific Research, the School of Aerospace Medicine, and the Southeastern Center for Electrical Engineering Education for the opportunity to perform this research. Special thanks is also due to Maj. James Rock, Dr. Richard Miller and Dr. Harry Hughes for their suggestions and support.

## I. INTRODUCTION

Diisocyanates are used in the production of polyurethane products. They are extremely toxic compounds, producing lung effects and respiratory sensitization in man at air concentrations below 1 ppm. The Air Force uses large quantities of diisocyanates in two operations, aircraft painting (polyurethane paint) and in-place packaging (polyurethane foam). In both operations, diisocyanates are mixed with alcohols to form the polyurethane products as needed; thus, the possibility exists that unreacted diisocyanates will enter the worker's breathing zones.

The purpose of this research project has been the development of an air-sampling and analytical procedure which can be used by Air Force personnel in evaluating airborne exposures to diisocyanates. This method is needed since existing procedures are subject to numerous errors in both air sampling and analysis. A brief discussion of these procedures and their shortcomings follows.

Several methods are based upon conversion of aromatic diisocyanates to the corresponding diamines in a fritted bubbler (1-4). The diamines are diazotized, coupled with a chromaphore, and the products measured spectrophotometrically. These methods do not measure aliphatic diisocyanates because of lower reactivities of these compounds. Since many polyurethane paints employ aliphatic diisocyanates, this is a serious shortcoming. Furthermore, the use of a fritted bubbler for sampling is undesirable because it has capricious collection characteristics for aerosols, a physical form often encountered with airborne diisocyanates, and it is subject to breakage and spillage of the liquid contents. The analytical procedure cannot differentiate among the diamines produced during sampling, the amines already present from the reaction of the diisocyanate and water vapor (prior to sampling), and the other amines present in the air (Amines are often used in polyurethane systems as catalysts.).

More recent methods react diisocyanates with chromophore-containing amines in a bubbler followed by chromatographic analysis of the ureas produced (5-7). These procedures measure aliphatic as well as aromatic diisocyanates and, because a separation step is included, the product ureas can be differentiated from amines and other potentially interfering compounds. However, since bubblers are still used to collect the diisocyanates, these methods are subject to the sampling pitfalls listed above.

The research problem, as envisioned, has four components. First, a method must be developed which can collect either aromatic or aliphatic diisocyanates. Second, the sampler must efficiently collect either aerosols (produced by dispersion processes such as paint spraying, foam injection, etc.) or vapors (generated by vaporization or sublimation of diisocyanates from uncured systems). Third, the analytical method must be extremely sensitive since exposure must be measured at low levels (<0.01 ppm as vapors). Finally, the analysis must be specific for the diisocyanates investigated, i.e., not subject to interfering compounds.

The proposed collection method draws air through a high-efficiency filter which has been impregnated with a chromophore-containing amine. Diisocyanate vapors react with the amine to produce a nonvolatile, unreactive urea. Diisocyanate aerosols are efficiently trapped by the filter. Any vapors released from trapped particles also react with the amine.

The proposed analytical method employs high performance liquid chromatography (HPLC) to separate the product urea from the amine used as the reagent and from other potentially interfering compounds. Detection employs UV photometry at the absorption maximum of the urea to ensure sensitive analysis.

## II. OBJECTIVES

Clearly, it was impossible to develop and evaluate a method for all of the diisocyanates used by the Air Force in 10 weeks. Thus, one compound, 1,6-hexamethylene diisocyanate (HDI) was selected for study. This diisocyanate is used by the Air Force in the largest quantity (paint systems). Furthermore, because it is an aliphatic diisocyanate, a successful method would also be applicable to aromatic diisocyanates which are much more reactive, and therefore easier to collect by the proposed sampling procedure.

The objectives of this project were:

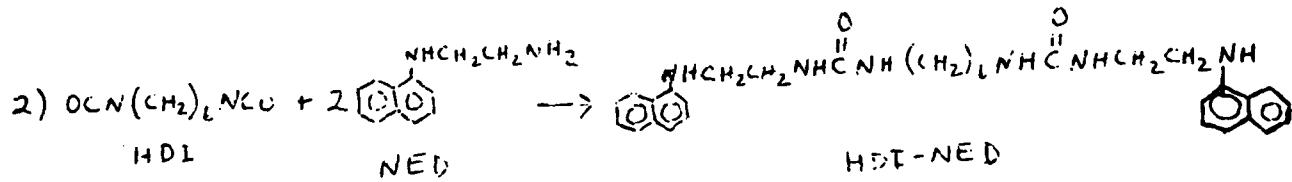
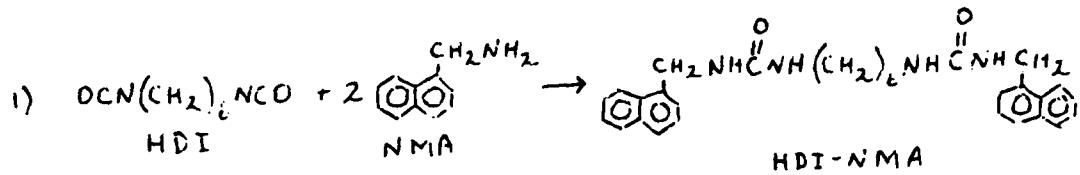
- 1) To select a chromaphore-containing amine(s) which reacts rapidly with HDI at room temperature and produces a urea which can be sensitively detected by UV photometry,
- 2) To characterize the urea(s) produced by reaction between HDI and the amine(s),
- 3) To develop a HPLC procedure which separates the urea from the amine and impurities,
- 4) To collect HDI vapors from an airstream by an amine-impregnated filter and recover the product urea in high yield.

## III. SELECTION OF THE REAGENT AMINE

In order to collect diisocyanate vapors from air successfully, the reagent amine must react very rapidly with these compounds. Whereas secondary amines will react with aromatic diisocyanates, only primary amines react rapidly with aliphatic diisocyanates (8-10). For instance, the reaction between HDI and nitro reagent, a secondary amine (N-4-nitrobenzyl-N-n-propyl-amine), required over 40 min. in liquid solution to go to completion (10).

Reactions between nitro reagent and several aromatic amines were virtually instantaneous (10). The reaction rate is also influenced by steric effects; thus, the carbon adjacent to the amino group should not contain substituent groups (8,9). In addition, the amine molecule must contain a strong UV chromophore ( $\epsilon_{\text{max}} > 10^4$ ) to allow detection of small amounts of the urea.

Two amines were selected for study, 1-naphthalenemethylamine (NMA) previously used by Levine *et al.* for collecting airborne diisocyanates in bubblers (7), and N-1-naphthyl-ethylenediamine (NED). Structures of these compounds and the product ureas are shown in the following reactions:



Both of these amines absorb very strongly in the UV. Absorption spectra are shown in Figures 1 and 2. The maximum absorbance for NMA is at 223 nm ( $\epsilon_{\text{max}} = 8.8 \times 10^4$ ) while the maximum absorbance for NED is at 210 nm ( $\epsilon_{\text{max}} = 5.0 \times 10^4$ ).

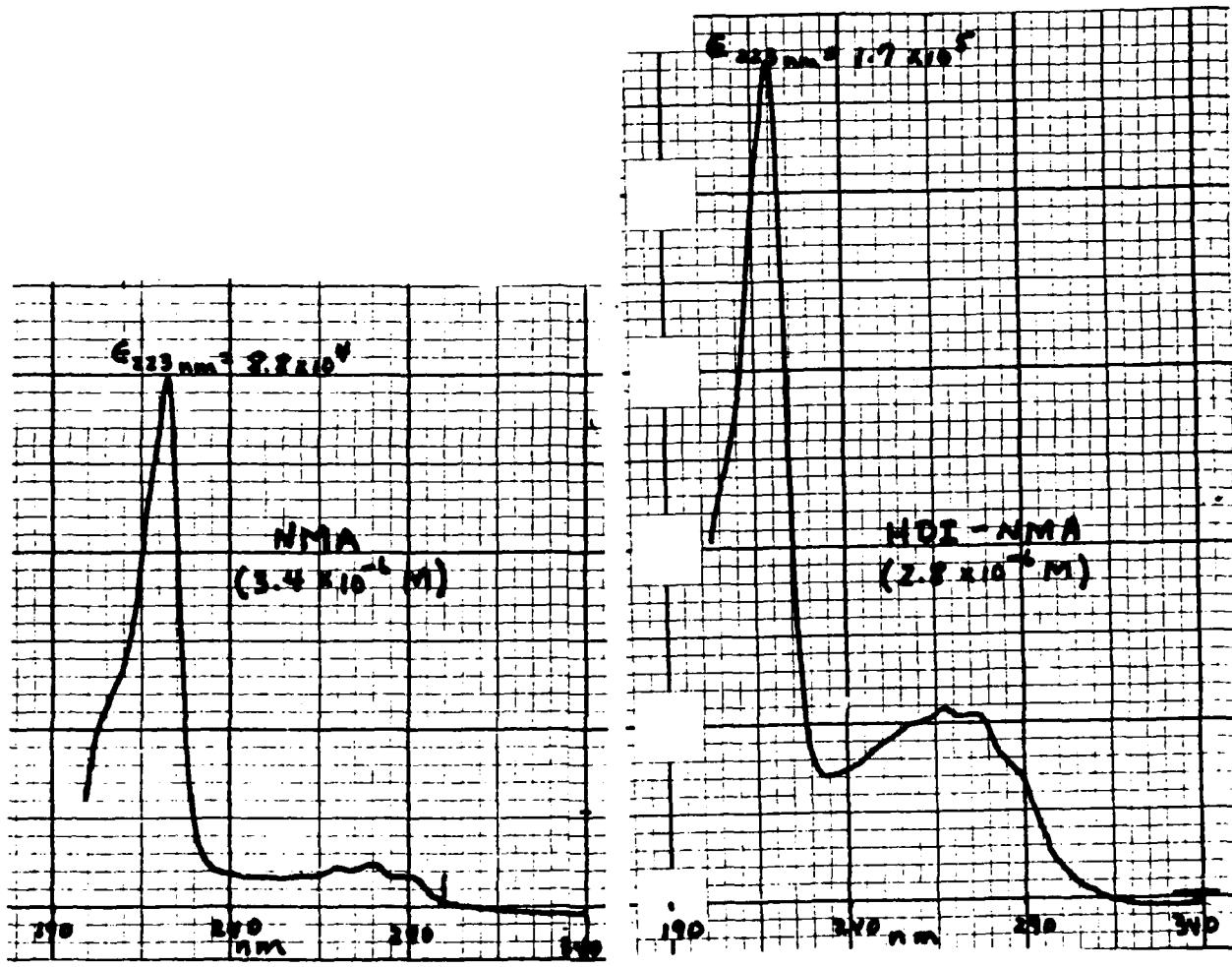


Figure 1. UV Absorption Spectra of NMA and HDI-NMA

**Conditions:**

Instrument - Beckman Acta III Spectrophotometer  
 Scan Rate - 0.2 nm/sec, 50 nm/inch  
 Slit Width - Programmed 0.6 nm at 340 nm, 1.5 nm at 190 nm  
 Range - 1 AUFS; Path Length - 1 cm; Solvent -  $\text{CH}_3\text{OH}$

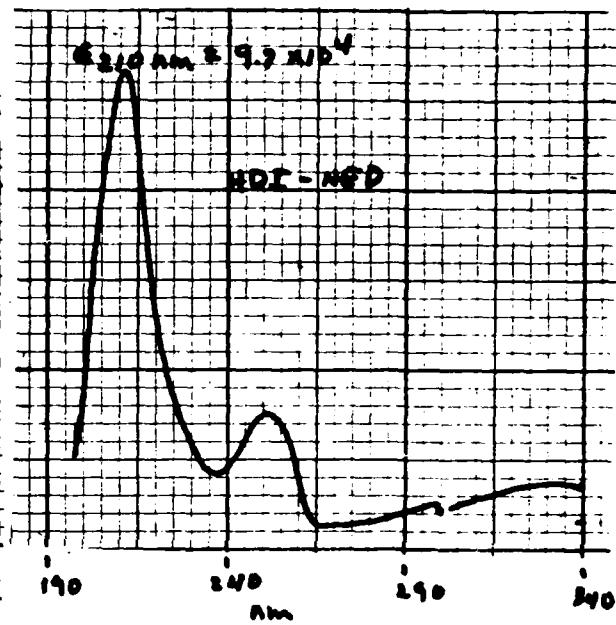
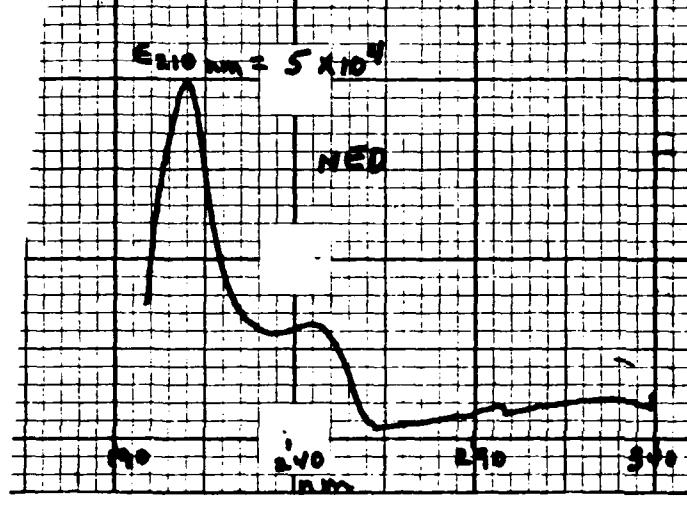


Figure 2. UV Absorption Spectra of NED and HDI-NED  
(Conditions same as given in Figure 1)

#### IV. PREPARATION AND CHARACTERIZATION OF UREAS

Ureas were prepared by reacting HDI with either NMA or NED in methylene chloride solution. 1.2 mmoles of NMA and 0.31 mmoles of NED were dissolved in 2 ml of methylene chloride in separate test tubes. HDI was injected directly into these solutions with a microliter syringe; 0.43  $\mu$ moles were added to the NMA and 0.13  $\mu$ moles were added to the NED. White precipitates were formed immediately. After standing for five minutes at 60°C, the methylene chloride was removed by evaporation under nitrogen. The products were filtered with glass-fiber filters, washed with methylene chloride to remove the excess amine, dried in a vacuum oven at 50°C and weighed. Recoveries were 0.40  $\mu$ moles of HDI-NMA (92% yield) and 0.10  $\mu$ moles of HDI-NED (77% yield).

The ureas were dissolved in methanol and the UV absorption spectra obtained. These compounds were soluble only at concentrations  $< \sim 10^{-6}$  M in methanol. Solubilities in other solvents (hexane, methylene chloride, acetonitrile, ethanol, water) were even lower. The absorption spectra are shown in Figures 1 and 2. They are qualitatively identical to the spectra of NMA and NED. However, the molar extinction coefficients (HDI-NMA  $\epsilon_{223\text{nm}} = 1.7 \times 10^5$ ; HDI-NED  $\epsilon_{210\text{nm}} = 9.7 \times 10^4$ ) are twice the values of the corresponding amines. This indicates that each molecule of the product does, indeed, contain two chromophore groups.

The melting points of the ureas were also measured. The melting range of HDI-NMA was from 245-248°C and of HDI-NED was from 189-191.5°C.

#### V. HPLC of HDI-NMA

Aliquots of HDI-NMA solutions were injected into an HPLC system, employing a variable-wavelength detector at the absorption maximum of 223 nm. The column was 30 cm x 4 mm-i.d. uBondapak-C<sub>18</sub> (Waters Assoc.) with a guard column containing Corasil-C<sub>18</sub> (Waters Assoc.). The mobile phase, consisting of 25% water/methanol, flowed through the column at 1.0 mL/min. Injections of 50  $\mu$ L were made with a loop injector.

Typical chromatograms are shown in Figure 3. HDI-NMA eluted at 6.2 min, well before NMA which eluted at 40 min. When the detector was operated at a range of 0.05 AUFS, the minimum amount of HDI-NMA which could be quantitated was ~ 2 ng corresponding to a solution concentration of 0.04  $\mu$ g/ml.

## VI. COLLECTION OF HDI IN AIR BY FILTERS IMPREGNATED WITH NMA

### A. Impregnation of Filters

Glass-fiber filters (Millipore Type AP, 37 mm) were dipped into a 0.396 mg/mL solution of NMA in methylene chloride. Preliminary trials showed that 1 mL was absorbed; thus, each filter contained 396  $\mu$ g of NMA. Filters were hung by metal clips to dry and stored at 0°C prior to use.

### B. Challenge of Filters with HDI Vapor

Impregnated filters were placed in standard 37-mm plastic, in-line holders. A glass tube was connected to the inlet of each holder so that air did not come in contact with the plastic as it entered. The outlet of the holder was connected to the inlet of a standard glass midget impinger containing 10 mL of  $10^{-4}$  M NMA in methylene chloride. Air was drawn through each sampling train at 0.3-0.4 L/min.

The experiment involved the addition of 6.13  $\mu$ g of HDI in methylene chloride solution to the interior of the glass inlet tubes of three samplers as air was drawn through them. Two control samplers were not spiked with HDI. Air was drawn through each train for 10 min. Subsequent analysis of the filters and impinger solutions for HDI-NMA would show whether or not all of the HDI had been trapped by the filter.

### C. Analysis of Filters and Impinger Solutions

Filters were removed from the holders and placed in 10-mL glass test tubes to which were added 6 mL of methylene chloride. Impinger

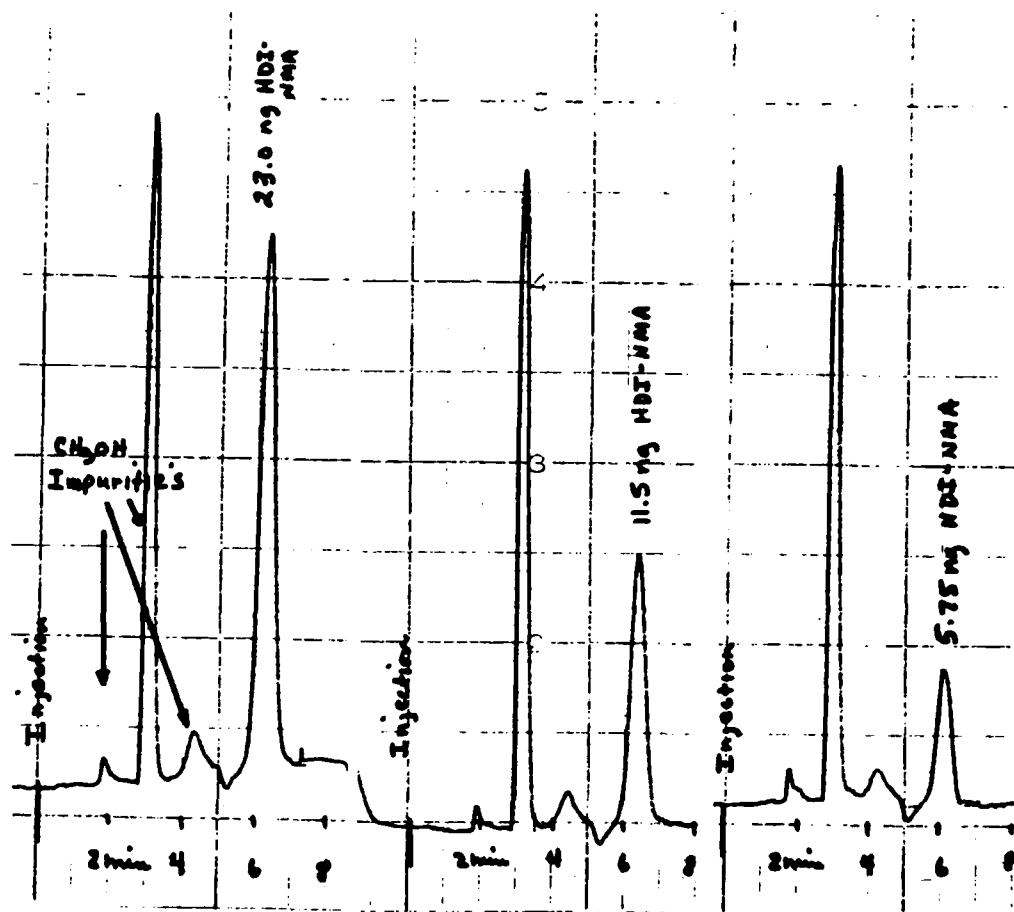


Figure 3. HPLC Chromatograms of HDI-NMA

**Conditions:**

Pump - Altex Model 100; Column - Waters  $\mu$ Bondapak C<sub>18</sub>  
 Detector - Altex/Hitachi Model 100-10 at 223 nm, 0.05 AUFS  
 Mobile Phase - 25% H<sub>2</sub>O/CH<sub>3</sub>OH at 1.0 mL/min  
 Injection Volume - 50  $\mu$ L; Solvent - CH<sub>3</sub>OH

solutions were also placed in test tubes. The solvent was removed from all samples at 40°C under nitrogen. Eight mL of methanol were added to each tube which was then capped and placed in an ultrasonic bath for 2 hr to dissolve the HDI-NMA. Aliquots of each sample were injected into the HPLC as previously described at a detector range of 0.05 AUFS.

#### D. Results

Data are shown in Table 1. HDI-NMA was found on the filters only; none was observed in downstream impingers. The mean recovery from the three filters in the experimental group was 18.0 µg. Since 6.13 µg of HDI produces 17.6 µg of HDI-NMA ( $6.13 \mu\text{g HDI} \times \frac{482.6}{168.2} = \text{M.W. of HDI-NMA}$ ) upon reaction with NMA, the mean recovery was 102%. This indicates that the filters quantitatively trapped the HDI vapors and that the urea was subsequently recovered without loss.

The quantitation limit at a detector range of 0.05 AUFS was 2 ng of HDI-NMA. If the HDI-NMA was dissolved in 4 mL of methanol, then the sensitivity of the method would be 0.16 µg/sample. This corresponds to an air concentration of 0.016 mg/m<sup>3</sup> or 0.0023 ppm in a 10 L air sample. This is well below the 1978 Threshold Limit Value for 2,4-toluene diisocyanate (TDI), the most toxic of the diisocyanates, which is 0.02 ppm. Relatively straightforward improvements in analytical procedures should further reduce the quantitation limit by a factor of 10.

#### VII. RECOMMENDATIONS

This research has clearly shown the viability of the proposed sampling technique for diisocyanates. With additional development a valuable monitoring method should emerge which allows the evaluation of airborne exposures to personnel working with diisocyanates. To reiterate, the advantages of the proposed technique with respect to existing methods are:

TABLE 1  
HDI-NMA RECOVERED FROM IMPREGNATED FILTERS  
AND IMPINGER SOLUTIONS (ND = not detected, <0.1 µg)

<u>No</u>	<u>Sample Type</u>	<u>HDI-NMA Found (µg)</u>	<u>% Recovery</u>
1	Filter	19.3	110
	Impinger	ND	
2	Filter	17.8	101
	Impinger	ND	
3	Filter	17.0	96.6
	Impinger	ND	
4*	Filter	ND	
	Impinger	ND	
5*	Filter	ND	
	Impinger	ND	

\*Control

- 1) The method should be appropriate for either aliphatic or aromatic diisocyanates,
- 2) The method should collect the airborne diisocyanates as either aerosols or vapors,
- 3) The method can differentiate the urea formed in the sampler from amines and other potentially interfering compounds, and
- 4) The sampler is simple, employs no liquids and is compatible with existing personal sampling equipment.

Additional research should be performed to validate the proposed method for HDI and other isocyanates used by the Air Force. Points which should be included in this validation program are:

- 1) Further evaluation of the method with HDI:
  - a) Test the sampling method with dynamic test atmospheres of HDI for both long and short-term sampling intervals,
  - b) Determine whether humidity influences the collection characteristics of the sampler,
  - c) Determine the storage stability of the samplers and the ureas after collection,
  - d) Determine the absolute sensitivity of the analytical procedure,
  - e) Streamline the chromatographic analysis to reduce the time required to elute NMA from the column, and
  - f) Collect samples during actual exposures to ensure that compounds present in the environment do not interfere with the method.
- 2) Evaluation of the method for other diisocyanates:
  - a) Synthesize and characterize the ureas produced upon reaction of the diisocyanates with NMA,
  - b) Evaluate the procedure with each compound as suggested for HDI (above), and
  - c) Determine whether those diisocyanates which are predominantly present as aerosols behave as predicted upon collection.

## REFERENCES

- 1) K. Marcali, "Microdetermination of Toluene diisocyanates in Atmosphere," Anal. Chem., Vol 29, pp 552-558, 1957.
- 2) K.E. Grim and A.L. Linch, "Recent Isocyanate-In-Air Analysis Studies," Am. Ind. Hyg. Assoc. J., vol 25, pp 285-290, 1964.
- 3) D.W. Meddle and R. Wood, "Apparatus for Preparing Standard Aerosol Atmospheres," Chem. and Ind., vol 47, pp 1635-1637, 1968.
- 4) D.W. Meddle and R. Wood, "A Method for the Determination of Aromatic Isocyanates in Air in the Presence of Primary Aromatic Amines," Analyst, vol 95, pp 402-407, 1970.
- 5) J. Keller, K.L. Dunlap and R.L. Sandridge, "Determination of Isocyanates in the Working Atmosphere by Thin-Layer Chromatography," Anal. Chem., vol 46, pp 1845-1846, 1974.
- 6) K.L. Dunlap, R.L. Sandridge and J. Keller, "Determination of Isocyanates in Working Atmospheres by High Speed Liquid Chromatography," Anal. Chem., vol 48, pp 497-499, 1976.
- 7) S.P. Levine, J.H. Hoggatt, E. Chladek, G. Jungclaus and J.L. Gerlock, "Determination of Aliphatic Isocyanates in Air by a Liquid Chromatographic-Fluorescence Technique," Anal. Chem., vol 51, pp 1106-1109, 1979.
- 8) D.J. David and H.B. Staley, Analytical Chemistry of the Polyurethanes, vol XVI, Part 3, New York (Wiley-Interscience, 1969), pp 215-217.
- 9) J.H. Saunders and K.C. Frisch, Polyurethanes Chemistry and Technology Part I Chemistry, New York (Interscience, 1962), pp 173-180.
- 10) C.R. Hastings-Vogt, C.Y. Ko and T.R. Ryan, "Simple Ureas Derived from Diisocyanates and their Liquid Chromatography on a 5-cm Column," J. Chromatog., vol 134, pp 451-458, 1977.